Title: The feasibility and effectiveness of PASS PLUS, a lay health worker delivered comprehensive intervention for Autism Spectrum Disorders: pilot RCT in a rural low resource setting

Background

Autism Spectrum Disorders (ASD) is a priority condition in low resource settings, with a global prevalence of approximately 1%, and a minimal evidence base for community interventions that can be delivered at scale in these settings [1, 2]. As a way to address this "treatment gap" for interventions delivered in the community, an international groupof collaborators systematically adapted PACT, an evidence-based communication intervention originally developed for delivery by specialist speech and language therapists in the UK [3], for delivery through the process of task sharing to non-specialist workers in two countries in South Asia [4]. 'Task shifting or task sharing' is recommended by the World Health Organisation and aims to address the severe shortage of a specialist workforce by allocating healthcare tasks in such a way that less qualified and more affordable workers can be trained to deliver components, under the support and supervision of more skilled specialists, to improve access and cost-effectiveness. The resultant Parent mediated intervention for Autism Spectrum Disorders in South Asia (PASS) was evaluated through a randomised control trial with 65 children with autism and their families, in two sites in Pakistan and India [5]. The PASS trial demonstrated the acceptability and feasibility of the intervention in the South Asian context, with 81% of participants completing the intervention sessions successfully. Significant treatment effects were seen in the primary outcomes of parent synchrony (ES 1.61, 95% CI 0.90, 2.32) and child initiation (ES 0.99, CI 0.29, 1,68) within dyadic social interactions.

In addition to these measured communication outcomes, however, the trial also identified considerable unmet needs of families in this context in addressing co-existing conditions

known to commonly occur with ASD; for example, behavioural and eating problems. Though prevalence rates applicable to high income countries (HIC) vary across studies, there is a high rate of comorbidities generally reported in children with autism across the ages; these include anxiety, sleeping, feeding, mood and behavioural problems (e.g., hyperactivity)[6]. One survey found that over fifty per cent of parents described their children as having more than four comorbid problems, with such comorbidities also impacting parental health[7, 8]. Evidenced management of these comorbidities in HIC, ranges from parent psychoeducation and training to medication [9, 10]. In the PASS pilot trial, the presence of comorbidities often preoccupied parents and, on occasion, interfered with their ability to engage with the home programs for core social communication symptoms, which were targeted in the PASS intervention. These comorbidities can further impact the autistic child's functioning, and participation in social and educational settings, as well as that evidence-based practices for such co-morbidities be used[11], with appropriate adaptation for the autism context.

To address the identified need, systematically developed a series of therapeutic modules for the most common comorbidities, which could be integrated efficiently into the core PASS social communication intervention and be delivered modules with the already proven core social communication intervention (PASS), was to create a holistic intervention package of care for families of children with ASD (PASS Plus), amenable to delivery by a lay health worker in low resource settings.

Methods

1) PASS Plus Manual Development

The first step was to identify the common comorbidities which families of children with Autism experience, and the approaches, theoretical underpinnings and delivery processes of interventions designed to address these comorbidities. The aim was to build on the broad recommendations given by the National Institute of Clinical Excellence 2013 guidelines, which separate the interventions for core symptoms from those of the comorbidities. Information from the three methods below was triangulated to develop comorbidity modules for the Indian context,.

1) ***Literature review***: A grey literature review was carried out to screen training manuals, information guides and published research articles on interventions for co-morbid conditions in ASD, which were written in English, Hindi, and Marathi. Searches were made in popular Autism websites, an automated search of electronic databases (Pubmed, Medline, Cochrane, EMBASE) was conducted and key informants were contacted. Any interventions for ASD which solely focused on language and communication or required medication were excluded. This process revealed the following relevant resources: 21 research articles, one workshop manual, 45 hand-outs or fact sheets, 10 manuals and 19 relevant websites.

2) ***In-depth interviews*** (IDI) (n=11) were conducted with lead clinicians of 11 premier institutions in the region (9 from India and one each from Bangladesh and Sri Lanka) in order to identify India context-specific aspects of co-morbidity. These were conducted by senior investigators (GD and PC). A semi-structured interview guide was developed which allowed the exploration of the context of work, the age of children with autism treated in the individual contexts, the common comorbidities observed, and the current management of these comorbidities. The aim was to describe common approaches that were considered acceptable and feasible in a low resource context.

3) Theory of Change (ToC) workshop: Senior clinician VV conducted one ToC workshop[12] with parents (n=14) of children with ASD in the district of Kolhapur, in the state of Maharashtra, India, where the proposed trial was to be conducted. The aim of this workshop was to determine the key unmet needs of families of children with ASD in the trial area, to gather information on parents' views on successful culturally appropriate treatment approaches for co-existing problems and to identify practical flow issues on delivering a comprehensive home based intervention by lay health workers.

All materials from the literature review were examined by senior researchers (PC, VV, GD). Themes were identified across the materials and framework illustrating the commonly described co-morbidities was developed. Each researcher then independantly plotted intervention strategies from the source material within this framework. These were compared across researchers and consensus was reached on the most scalable strategies.. All interviews were in English (PC, VV, GD) and were transcribed using the expanded notation methodology. Using the framework developed above, two interviews were double coded by senior researchers (PC, VV and GD). A consensus coding was developed and then the researchers (VV and GD) worked independently to incorporate all strategies and approaches described in the interviews and the workshop into this framework. Interviews with lead clinicians revealed that they were identifying similar comorbid conditions across the centres, notably aggression and self harm behaviours, hyperactivity, sensory issues, feeding and toileting difficulties and maternal stress. This matched information obtained from parents. Clinicians also reported addressing anxiety, depression, bipolar disorder and obsessive-compulsive disorders; however, such comorbidities were seen to be beyond the capabilities of the task sharing approach. The outcome of the analyses described above was a list of those comorbidities which could be addressed by psychosocial approaches (e.g.

behavioural disruptions and sensory integration problems) and would be amenable to task sharing with lay health workers.. Data triangulated from these methods were presented to a range of national ASD experts in an Intervention Development Workshop.

4) Intervention Development Workshop: The 20 participants included special educators, occupational therapists, developmental paediatricians and clinical psychologists from across India. The aim was to develop a theoretical framework for the comorbidity intervention, which built upon the findings of the preceding steps. The workshop also aimed to elicit participant views on the required competencies of the lay health worker, their training and supervision. The result was a framework of additional modules (the 'Plus' modules), which could be grafted on to the core PASS communication intervention and be delivered through the process of task sharing with a lay health worker, under supervision of a specialist. Table 1 describes the comorbidities addressed and the overview of each module. Each module was thus based on the inputs of experts, extracted materials from the literature review and the theory of change workshops. In addition an initial comorbidity screening questionnaire for parents, was adapted from work done in the United Kingdom [7]. The Plus component uses a simple decision support algorithm, which commences by defining the various comorbidities that a parent is concerned with using the screening questionnaire. These are then prioritized based on their frequency, severity and disruption to daily life. Each module has been developed so that a further decision support algorithm allows for the tailoring of the intervention to the needs of the individual family. For example, if sleeping issues are prioritized, the parent is asked to identify the nature of the sleep problem and is requested to keep a simple sleep diary. This is then explored in the subsequent sessions by the lay health worker who uses the decision tree to identify specific strategies . These may include, in this

example, creating a calming sleep routine, adaptations in the sleep environment or avoiding day time naps.

Table 1 about here

2) Randomised Controlled Trial

Design

This was a two arm single (assessor)-blinded randomised controlled trial of the PASS Plus intervention against usual care. The trial was carried out in the district of Kolhapur in the southwest part of the western state of Maharashtra, India. Kolhapur city serves as the headquarters of the Kolhapur district with a population of 3,876,001, of which 68% is rural. A government medical college and a district hospital are located in Kolhapur city, but no autism specific services are available for diagnosis and treatment of autism within the public sector. Some families are able to access diagnostic services through private psychiatrists and paediatricians or at the two private child development centres, which provide a multi-modal service including behavioural modification, physiotherapy, and speech and language therapy. There are no community-based services for the early detection or management of autism, and no family support.

Families of children with autism were recruited through a community screening program conducted as part of a larger community engagement initiative, as well through child development clinics, and special schools in the city of Kolhapur. Diagnostic evaluations were conducted using the INCLEN Diagnostic Tool for Autism Spectrum Disorder[13]. INDT-ASD is a diagnostic tool based on the DSM-IV criteria and is divided into two sections. The first section includes questions and supported observations around the three domains of social interaction, social communication, and restricted interests, while the

second section allows a differentiation in to diagnostic categories. The tool has been found to have good psychometric properties and is recommended by the Ministry of Social Justice and Empowerment, Government of India. For the trial, children aged 2-9 years old (mean age 64 months; range 27- 105 months) were initially assessed to ensure that their developmental age was equivalent to 12 months or older, a criteria which permits engagement with the intervention materials. The developmental assessment screening administered was based on the stages of development in Gesell and Amatruda and the Mullen Scales of Early Learning [14, 15]. Exclusion criterion included uncontrolled epileptic seizures, severe hearing or visual impairment in the child or parent, a severe psychiatric disorder in the parent and residence outside the trial area.

The study received ethical approval from the Institutional Review Board of Sangath as well as from the Indian Council of Medial Research. Informed consent was obtained from one parent of every family participating in the trial. The trial registration number is ISRCTN10260663.

Randomisation and blinding: Following consent and registration with the site co-ordinator, participants were administered the baseline assessments. Sequential identification numbers were assigned to each child, which were then sent to the independent randomization centre at Sangath, Goa, India. Randomisation lists were stratified by age (below 5 years and 5 years and above) and functional impairment (on the Vineland Adaptive Behaviour Scales-Adaptive Behaviour Composite score[16]); these were selected as features that may influence the response to treatment. Allocation was conveyed by telephone and by email to the site coordinator who communicated with the intervention team. Research members of staff were masked to treatment allocation.

The research and intervention teams were housed in distinct site offices with separate supervisory staff. To mitigate any effects of the intervention arm children being familiar with the play materials, separate sets of toys were used by the two teams. To mitigate any systematic effects from familiarity with the videoing, which is intrinsic to the therapy, two additional video-recorded play sessions per participant were included in the treatment as usual group, 2 and 4 months after baseline assessments.

The baseline and endpoint measures (see below) were presented to the assessors as anonymised videos, without details indicating the arm of the trial or the time point of the assessment.

Intervention The 'Parent mediated intervention for Autism Spectrum Disorder Plus' (PASS Plus) treatment consisted of one on one home based sessions between the parent and the lay health worker. The intervention had two distinct components; the PASS social communication modules and the 'Plus' comorbidity modules. The core social communication intervention (PASS) aims to increase parental synchronous responses while simultaneously decreasing the directive parental approach by using video-feedback on play sessions recorded during a ten-minute period of play between the parent and the child. This manualised PASS intervention [5] is staged to represent a developmental progression of early social communication skills. The PASS facilitator visits the home of the child, gives the parent a standard box of toys and requests them to play with their child. The toys are selected taking into account the individual child's interests, which creates opportunities for interactive play. The ten-minute play session is video recorded. The PASS facilitator then reviews the video taken with the parent. Based on manualised instructions, the facilitator uses a reflective approach to support the parent to recognise the child's non-verbal and verbal signals, which reflect the child's communication intentions, and to recognise which

of their own actions have a positive effect on the interaction. The parent is then guided to try intervention strategies that aim to help the parent closely observe the child's intentions and interests, reduce their own demands and respond to the child with communication matched to the child's focus of interest and language levels. The individual strategies are naturalistic and include simple, but effective, strategies such as paying attention to parent positioning, watching and waiting and reducing the use of questions and directives. Parents choose strategies to try out at home and the effect of these on their dyadic interaction is reviewed at the start of the next session.. This part of the session takes less than one hour. The novel Plus modules are delivered using a manualised clinical decision algorithmic approach and address common comorbidities using a psychosocial approach. Figure 1 illustrates the staged delivery of the PASS and Plus modules in the intervention arm. The Plus modules are introduced in the fourth session, after the facilitator and parent have established an alliance, allowing the probing of sensitive issues including parental mental well being. After supporting the parent to identify the co-morbidity most disruptive for the family, the decision algorithm enables the facilitator to identify the most relevant advice and strategies for the family. The modules take approximately 15-30 minutes to administer and their content is described in Table 2. Parents are given a personalised written home practice sheet for both components of the intervention and are requested to practice the communication strategies for 30 minutes every day in the intervening fortnight. The pace of the progression across PASS stages is guided by each parents' abilities to use the strategies suggested.

Figure 1 about here

Methods of training and supervision for the core communication component were developed and refined in the original PASS trial. For this trial, intervention and training materials were

translated into the local language Marathi. The lay health workers, who were college graduates without any specific training in child development, received a 10-day curriculum which included classroom based instruction on child development and autism, observations in special education settings of children with social communication impairments, and practice based learning of the modular intervention PASS. The senior clinicians on the project, along with the mid-level supervisor, conducted the training and supervision of the lay health workers. A first stage competency measure evaluated the knowledge and skills of the selected candidates, who were then allowed to co-deliver the intervention to non-trial practice dyads under supervision. During the one-month internship period, each trainee delivered a minimum of 3 sessions independently after which a second level objective competency measure was administered on PASS specific knowledge and skills. Of 5 trainee candidates, 4 achieved a pre-determined competency score and then engaged with trial dyads. Two months into the case practice sessions the lay health workers received an additional two-day training on the Plus modules.

The intervention delivered consisted of 12 fortnightly sessions in the families' homes over a 6-month period. The first session on engagement was conducted with a Supervisor present. The supervisor was a specialist in the management of autism and a master trainer for the PASS intervention. This allowed a more skilled person to explore family beliefs around the intervention, which could impact the family engagement with the intervention. As indicated in intervention flow diagram in Figure 1, parents were administered a questionnaire on the impact of the comorbidities in Session 4 of the intervention which guided the lay health worker to the appropriate Plus module. All sessions were video taped and these were used initially for one-on-one supervisions by PASS Plus trainers. All intervention sessions were conducted in the local languages of Marathi or Hindi, for which language specific manuals

were developed. The pattern of supervision over the trial period evolved from an initial high intensity group supervision conducted once a week by a senior clinician to peer led supervision. All supervision sessions used a quality measure standardised in the previous trial. This measure, the PASS Plus Rating Scale, assesses generic counselling skills as well as skills required to deliver a PASS Plus session. Self-scoring and scoring peers allowed the lay health workers to build critical skills and adopt a more interactive role in supporting each other in peer supervision sessions. These were then supervised every fortnight by the senior clinicians. The focus of the supervision also evolved from skill building, particularly in supporting the lay health workers to identify the best segments of the videos, to an emphasis on a more problem solving approach. Adherence of the implementation team was rated on fidelity measures developed previously[3]. These were conducted by a therapy expert based in the UK (CT) on 10% of randomly selected treatment sessions (24 sessions, 6 from each facilitator in 3 tranches over the trial period).

All families, whether in the intervention or control arm of the trial, continued with the usual treatments in which they were engaged. The intervention arm dyads received the PASS plus intervention in addition to their usual care.

Outcomes

Autism symptom severity, using the Brief Observation of Social Communication Change (BOSCC)[17]. The BOSCC has been developed by the originators of the standard diagnostic instrument, ADOS [18], with the aim of being a measure of autism symptom behaviours which is sensitive to nuanced change over a relatively short period of time and thus appropriate for intervention outcomes. It codes across 12 behaviours, which include the quality of eye contact, the kind of play observed, gestures made and words directed at the

adult during two video recorded short periods of play. Unlike the ADOS, the play is not carefully structured or led by an administrator but is conducted as a more naturalistic interaction between the administrator and the child. The 0-5 scale (total 0-60) for the 12 items has also been developed to be administered and coded by non-specialists. This makes it highly suitable for low and middle income country (LMIC) implementation, and this trial was its first usage in this setting. The BOSCC shows excellent inter-rater reliability, satisfactory-excellent internal consistency and good test-retest reliability [19, 20]. There is less data to date on concurrent or criterion validity, although overall correlation with ADOS is generally reported. The instrument development team from the US trained master trainers from India (GD, PC), who undertook an adaptation for the South Asia context (including simplified behavioural descriptions and visual aids), and trained the trial Research Assistants (RAs) who had minimum prior exposure to autism. Coding of the BOSCC within the trial was shared by two project RAs and a US master coder. The inter-rater reliability (n=16; comparing 2 trial RAs with the US master coder) gave an ICC of 0.80

Dyadic social communication, using the Dyadic Communication Measure for Autism (DCMA)[21].The DCMA is a widely used measure of parent-child interaction that in previous studies[3, 5] has shown excellent feasibility of use in the Asian context, inter-rater reliability and sensitivity to treatment effect change. The DCMA is coded from an 8 minute video made of a naturalistic parent-child play session with a different box of toys. Separate videos were made for the administration of BOSCC and DCMA, but on the same day, thus minimizing inconvenience for families. The DCMA tapes are coded for communication acts, which may be verbal or non-verbal. The parent variable is synchrony i.e., the proportion of parent communication acts with the child that were synchronous. Synchronous acts are responsive, undemanding contingent and relevant to the child's focus -(for example,

acknowledging the child or making a comment about their play), asynchronous acts place demands on the child or are not contingent with the child's focus or interests (for example, commands, requests or re-directions). The child variable is child initiations i.e. the proportion of child responses that were communication initiations. A dyadic variable, mutual shared attention, is also coded; this is the proportion of interaction time that the parent and child spend focused on the same action or toy.. In our trial, inter-rater reliability of 94 % across the DCMA codes was established between the two coders on a sample of 8 practice clips; these two coders subsequently coded the DCMA in the trial. The within trial inter-rater reliability (n=28; comparing 2 trial RAs gave an ICC of 0.90 on parent acts (synchronous and asynchronous), 0.93 for child communication initiations and 0.96 for time in mutual shared attention. Fidelity checks were done for on a random sample of 4 clips for each coder (approx. 10% of the total trial clips) over the course of the trial.

Mental Health Comorbidity, using the Developmental Behaviour Checklist (DBC)[22], a standardardised parental interview specifically designed for use in developmental disability and extensively evaluated in learning disability and autism.

Adaptive child behaviours, using the standard Vineland Adaptive Behaviour Scale (VABS).[16]

Parental mental well-being, using the PHQ-9 a tool which has been validated and used in the extensively in the region[23].

Parent self-perception of knowledge, skills, acceptance, empowerment and advocacy using a measure adapted from the Research on Autism and Families in India (RAFIN) study[24].

The RAFIN tool was adapted for this study to reflect key areas in which parents could show changes through their engagement with the PASS Plus intervention namely; parent knowledge in understanding how autism impacted their child's communication; parent acceptance of their child's atypical behaviours; parent empowerment in independently seeking out help for problems related to their child's autism and parent involvement in any advocacy activities. The tool was a 19-item parent questionnaire in these four domains, with Likert scale responses, to generate a total of 97.

Statistical Analysis

Analysis followed the intention-to-treat principle. Outcomes were analysed using linear regression (ANCOVA), with the baseline measurement of the outcomes and treatment assignment as fixed effects. The linear regression models allowed analysis of all available data for primary and secondary outcomes without imputation, under the assumption that data were missing at random, conditional on the covariates. All models were bootstrapped with 250 replications. We report estimated adjusted mean differences as treatment effects, with their bootstrapped SEs, 95% confidence intervals, and Cohen's d effect sizes. The statistician was masked to treatment allocation during the analysis.

Results

Figure 2 shows the CONSORT diagram of participant flow through the study. A total of 5/40 (12.5%) subjects (4 from intervention and 1 from TAU) were lost from follow-up.

Baseline characteristics: Baseline characteristics are shown in Table 2 and baseline scores in clinical measures in Table 3.

Receipt of PASS intervention: 17/19 (89%) dyads received at least the minimum dosage of 3 sessions and 13/19 (68%) received the maximum 12 sessions of the core PASS communication intervention; 2/19 (10.5%) dyads discontinued and received <3 sessions. The PASS Plus comorbidity modules were delivered to 15/19 (79%) dyads; for the remaining 4/19 (21%) the session 4 questionnaire indicated no expressed need for Plus module intervention. The most commonly delivered modules were Behavioural Problems (in 12 cases over an average of 3.25 treatment sessions each), Sensory Difficulties (7 cases, average 2.3 sessions), Toileting (5 cases, average 2 sessions), Maternal Well being (4 cases, average 1 session), Sleep (3 cases, average 2.7 sessions) and Feeding (2 cases, average1.5 sessions). For the core PASS procedures, twenty-two of the 24 sessions checked (92%) met the required item and mandatory content thresholds for fidelity and 23/24 (96%) for session quality. For the Plus modules (rated separately since they were new, on sessions where they were used), equivalent fidelity thresholds were reached in 12/16 (75%) sessions and quality criteria in 13/16 (81%).

A focus group discussion at the end of the trial with the lay health workers allowed the team to explore their challenges and successes in the task sharing model. All four described how their initial anxieties around the home delivery model were allayed over time, with most target families welcoming them into the home for sessions. One particular challenge arose from a well-informed mother whose knowledge base on autism challenged the lay health worker's own more limited understanding. However, this mother was reassured when the nature of task sharing, which allows access to the supervisor to help address more complex challenges, was explained. The lay health workers also felt that, though the Plus modules lengthened the time within sessions, the majority of families had welcomed the additional strategies.

Receipt of usual car: Both arms were able to access regular treatment: in the intervention arm, 9/19 (47%) children visited allopathic private doctors (3 visits [1–9] in 6 months) while 3/19 (16%) visited Ayurvedic/homeopathic doctors (2 visits [1–3] in 6 months). In the control arm, 12/21 (57%) children visited allopathic private doctors (2 visits [1–9] in 6 months) while 9/21 (43%) visited Ayurvedic/homeopathic doctors (3 visits [1–8] in 6 months). 1/21 (5%) had received treatment from traditional practitioner. None of the families were receiving speech and language therapy, occupational therapy or physiotherapy during the trial period. 3/19 (16%) children in the intervention arm attended a specialist school (20 h [13–30] per week) and seven (37%) attended a mainstream school (23 h [12–36] per week). In the control arm, three (14%) of 21 children attended specialist schools (34 h [17–48] per week) and twelve (57%) attended mainstream schools (19 h [6–36] per week), while 1 (5%) child had a home tutor. Specialist and mainstream schools offered largely respite care with some remedial education, with no notable specific intervention for autism.

Outcome estimation

Table 3 shows the mean scores by arm, the adjusted mean difference, and Cohen's d effect size for all outcomes. An effect of -2.42 and ES of 0.22 for the BOSCC total score reflects a reduction of symptom severity in favour of the PASS Plus intervention, though the variance is high and the confidence intervals include zero, ranging from substantive reduction to modest increase. This between-group effect is accounted for by an increase in symptom severity in the control arm compared to little change in the intervention arm. Dyadic social communication results on the DCMA show an effect size in favour of PASS Plus on both proportion of parent synchrony responses and on proportion of child communication initiations. Time in mutual shared attention shows a small effect in favour of the intervention, but with confidence intervals that cross zero. Results on total DBC score show

no evidence of between-group difference. The pattern of effects on parental mental health and self-concept measures indicates the possibility of treatment effect. The PHQ9 measure of mental health shows between group difference in favour of intervention, though also with confidence intervals that cross zero..On the RAFIN measure, findings on the acceptance and empowerment scales show a difference in favour of treatment but again with wide CIs that contain zero.

Table 3 about here

Discussion

We report on the systematic development, through a series of formative research methods, and the evaluation through a pilot RCT, of the PASS Plus intervention for autism and associated co-morbidities. In summary, we observed high levels of feasibility of delivery by lay health workers (reflected by high fidelity of the intervention delivery) and favourable effects on the autism, dyadic social communication and maternal mental health outcomes. Though acceptable, we observed lower fidelity for the newer Plus modules, in particular due to the extent to which the lay health workers were able to tailor delivery to the family's needs. Modifications to the support algorithms and enhanced training and supervision are planned so as to improve fidelity in the implementation of these modules. Full details available from the authors.

The PASS Plus study extended the original PASS study in four key ways: 1) by adding modules to address common co-morbidities associated with autism in order to create a comprehensive package of care; 2) by implementing the intervention in a more demanding setting in rural India, with less health support infrastructure than was the case in either Goa

or Rawalpindi in the original study; 3) by pilot testing the delivery of comorbidity extension to the intervention in a way that could be managed by local health workers using a decision support algorithm; and 4) by piloting, for the first time in a LMIC, the new BOSCC instrument as a measure of autism symptoms. These extensions aimed to make the PASS Plus intervention more comprehensive and applicable in the most demanding of health settings whilst increasing rigour and comparabilityof the trial to the UK PACT trials[25], through the measurement of autism symptom outcomes in addition to the proximal intervention outcomes of dyadic social communication.

The intervention was successfully delivered in this rural context, in spite of the fact that the supervision structure originally developed in the PASS trial was more challenging to implement in this larger rural area. Five of nineteen families in the active treatment group were lost to follow-up (Figure 2), with two of those losses related to the intervention (one father withdrew consent and the second was a family who expected a traditional child directed therapy approach) and the rest to extraneous circumstances (ill health and families moving out of trial area). These findings support the overall success in acceptance and adherence for this new treatment in a rural setting, though a definitive implementation trial would allow the assessment of effectiveness and of key challenges and facilitators at scale. The comorbidity modules were used in the majority (79%) of cases, with a good spread across the comorbidities targeted; suggesting successful incorporation of this new element into the treatment. Crucially, inclusion of the comorbidity modules did *not* lead to a reduction of the quality or effectiveness of the core social communication intervention (a theoretical concern in the design stage). As evidence, adherence to the intervention was comparable to the PASS trial and the dyadic outcomes are very similar. Experience from the delivery of the new comorbidity modules will be relevant to further refinements of the

method for future work. We also showed the feasibility of successfully delivering an RCT in this context to good internal validity; measurement of adjunctive usual care shows firstly a balance across the groups, and secondly how little autism specific therapy was available in this area of India.

We showed the feasibility of training and administering the new BOSCC measure of autism symptom severity by local research staff within the study setting. This represents the first time autism symptom outcomes have been assessed in a trial in LMIC. Given the sustained effect on autism symptoms now demonstrated in the original UK PACT intervention[25], this is an important outcome to assess for the effectiveness of autism interventions.

A potential limitation of this study is its generalizability in the context of the relatively high educational level of the mothers, which though reflective of the National Census data for this population, is not representative of literacy levels nationally.

There are a number of important conclusions from this randomised control trial of a complex intervention for autism in a low–resource setting. Firstly, although the trial was underpowered for definitive effect estimation, the pattern of point estimates is generally in a hypothesized direction indicating the effects of the intervention. Second as described above, the BOSCC is a tool that can be used successfully in a low resource setting; it did not show statistical significance but this could be expected, given the low power of this pilot trial. However, our results do show that the BOSCC is usable in this setting and could be included in larger trials. Third as in the original PASS and PACT trials, we have had strong effects in favour of the PASS Plus intervention on dyadic communication outcomes. This is particularly relevant for parental synchrony, which in the UK PACT trial showed a change

with positive cost effectiveness acceptability [26] and which mediated change in autism symptom outcome [27] – thus suggesting that the change found in PASS PLUS is likely to be a meaningful one.. Finally, the comorbidity modules did not affect fidelity or adherence to the core communication intervention, but the intervention did have some positive effects on maternal mental health outcomes.

While successfully demonstrating feasibility and adherence, the modest sample size of this pilot trial of PASS Plus makes it underpowered for any strong inferences regarding effectiveness. However, the fact the effects obtained were in a direction consistent with a positive effect of PASS PLUS intervention is encouraging for future larger scale work using these measures.

Acknowledgements

VP is supported by a Wellcome Trust Principal Research Fellowship. JG is a UK National Institute for Health Research (NIHR) Senior Investigator. The views expressed in this article are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health. We thank the Kolhapur Sangath team who rallied around to successfully deliver a complex trial and the many community members who enthusiastically came together to create awareness for autism in the community. We gratefully acknowledge the training, guidance and generous support of Professor Catherine Lord and her team in relation to the BOSCC measure. The study was funded by the Grand Challenges Canada Global Mental Health Stream. The funder had no involvement in the carrying out of the study, data analysis, interpretation or write-up.

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Table 1: Plus Modules

Module Focus	Module Content
Defining the comorbidity	Assessment General Psycho-education Priority setting
Comorbidity Management including targeted psycho-education	Sensory challenges • Strategies for sensory seeking and sensory defensive behaviours Behavioural challenges • Understanding the reasons for specific behaviours • Hyperactivity • Self harming and aggression • Transitioning challenges Sleep Problems • Sleep hygiene • Bed wetting Feeding difficulties • Restricted diets • Inflexible routines • Pica Toileting difficulties • Toilet training • Fear of toilets Parental well being • Mental health and hygiene

Table 2. Baseline Demographics of PASS Plus trial sample

Variable	Control (N=21)	Intervention (N=19)
Gender		
Male	19	15
Female	2	3
Unrecorded	0	1
Mother's education		
High school or lower	7	9
Undergraduate or higher	14	10
Age at demographics (months)		
Mean (SD)	65.6 (24.0)	64.3 (19.6)

Table 3: Outcome summary statistics by group & estimated adjusted mean difference with 95% confidence intervals

Outcome	Time	Control (n=21 enrolled; 20 at end-point)	PASS Plus (n=19 enrolled; 15 at end-point)	Treatment effect	
				Adjusted Mean Difference	
		Mean (SD)	Mean (SD)	Effect (Boot SE); [95% CI]	Effect Size
BOSCC average scores	T1	32.79 (8.88) (n=21)	36.26 (13.01) (n=19)	-2.42 (2.72) [-7.75, 2.92]	0.22
	T2	36.48 (12.37) (n=20)	35.93 (10.71) (n=15)		
DCMA: Proportion of parent synchronous responses*	T1	9 %(0.08) (n=21)	10 %(0.10) (n=19)	0.35 (0.09) [0.18, 0.52]	3.97
	T2	12% (0.12) (n=20)	46% (0.33) (n=15)		
DCMA: Proportion of child communication initiations*	T1	22% (0.17) (n=21)	18% (0.17) (n=19)	0.17 (0.07) [0.03, 0.32]	1.02
	T2	26% (0.20) (n=20)	42% (0.24) (n=15)		
DCMA: Proportion of time in shared attention*	T1	35% (0.21) (n=21)	35% (0.19) (n=19)	0.10 (0.08) [-0.07, 0.27]	0.50
	T2	54% (0.26) (n=20)	65% (0.25) (n=15)		
DBC: Scale total	T1	68.24 (28.43) (n=21)	58.38 (27.37) (n=19)	-9.00 (7.78) [-24.26, 6.26]	0.32
	T2	68.71 (28.15) (n=20)	55.80 (22.27) (n=15)		
VABS ABC Standard Score	T1	56.33 (10.88) (n=21)	58.53 (11.52) (n=19)	0.67 (2.28) [-3.80, 5.15]	0.06
	T2	60.53 (12.98) (n=20)	65.00 (12.69) (n=15)		
VABS Communication domain standard score	T1	54.43 (15.18) (n=21)	55.95 (16.73) (n=19)	2.63 (2.41) [-2.09, 7.36]	0.17
	T2	55.90 (14.15) (n=20)	60.93 (17.88) (n=15)		
VABS Receptive subscale v score	T1	7.48 (3.97) (n=21)	7.47 (3.29) (n=19)	1.42 (0.81) [-0.16, 3.01]	0.39
	T2	7.70 (3.69) (n=20)	9.47 (4.49) (n=15)		
VABS Expressive subscale v score	T1	6.43 (2.91) (n=21)	6.84 (3.52) (n=19)	-0.25 (0.43) [-1.08, 0.59]	0.08
	T2	6.85 (2.66) (n=20)	7.20 (3.26) (n=15)		

VABS Written subscale v score	T1	8.84 (1.80) (n=21)	8.79 (3.07) (n=19)	0.74 (0.54) [-0.32, 1.80]	0.30
	T2	8.47 (1.71) (n=20)	9.20 (2.65) (n=15)		
VABS Socialisation domain standard score	T1	60.14 (8.77) (n=21)	61.32 (9.87) (n=19)	3.31 (2.90) [-2.38, 9.00]	0.36
	T2	63.25 (11.45) (n=20)	68.47 (10.26) (n=15)		
PHQ 9	T1	7.33 (7.04) (n=21)	4.58 (4.40) (n=19)	-4.55 (2.03) [-8.52, -0.58]	0.76
	T2	9.45 (7.36) (n=20)	4.00 (4.90) (n=15)		
RAFIN KSQ Knowledge and Skills	T1	31.52 (6.89) (n=21)	32.84 (4.83) (n=19)	0.13 (1.45) [-2.71, 2.97]	0.02
	T2	38.55 (6.75) (n=20)	38.53 (4.41) (n=15)		
RAFIN AS Acceptance Scale	T1	20.19 (3.50) (n=21)	18.74 (2.84) (n=19)	1.28 (0.75) [-0.19, 2.75]	0.39
	T2	20.20 (2.28) (n=20)	21.33 (1.84) (n=15)		
RAFIN ES Empowerment Scale	T1	9.90 (3.25) (n=21)	9.89 (3.54) (n=19)	1.13 (1.01) [-0.85, 3.11]	0.34
	T2	11.75 (3.85) (n=20)	12.53 (3.16) (n=15)		
RAFIN PAA Parent Advocacy Activity	T1	2.90 (1.51) (n=21)	3.42 (1.30) (n=19)	-0.15 (0.54) [-1.21, 0.92]	0.11
	T2	4.10 (1.89) (n=20)	4.27 (1.79) (n=15)		
RAFIN Total	T1	64.52 (10.90) (n=21)	64.89 (9.59) (n=19)	3.72 (2.38) [-0.93, 8.39]	0.37
	T2	74.60 (10.42) (n=20)	76.67 (7.66) (n=15)		

* See text for full definitions